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16. ABSTRACT

The influences of atmospheric sulfate aerosols -- when translated to acid rain -- have received much attention; in the past, most studies have been associated with botanical and wildlife issues. We shall consider a new risk assessment vector: the effect of 'acid air' on human health; specifically, regarding children by considering the effects of hygroscopicity upon aerosol deposition in the lung as a function of human subject age. Children are a critical sub-population to be incorporated into health effects analyses following ambient exposures. Sulfate particles are products of the combustion of fossil fuels --and are consequences of basic personal needs and industrial uses, and are prevalent in the atmosphere. Hence, they cannot be avoided by the general public and workers. We introduce experimental hygroscopic growth information into a validated mathematical model describing aerosol deposition in the human lung. The results are intended for hazard evaluations pertinent to humans subsequent to exposures to pollutant atmospheres. The influences of hygroscopic growth, taking place when inhaled particles enter the warm, moist human respiratory tract, are significant; and, should not be ignored in considerations of threat-to-human-health. Our findings can be directed into aerosol therapy functions also, leading to more efficient administrations of drugs via the inhalation route. Therefore, our findings, considering age-dependency, are of potential application to pediatric medicine.

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INTRODUCTION

The influences of atmospheric sulfate aerosols -- when translated to acid rain -- have received much attention; in the past, most studies have been associated with botanical and wildlife issues. Now, in our contribution to this international symposium, we shall consider a new risk assessment vector: the effect of 'acid air' on human health; specifically, regarding children.

We shall attempt to achieve our purposes by considering the effects of hygroscopicity upon aerosol deposition in the lung as a function of human subject age. Since children are a critical sub-population to be incorporated into health effects analyses (i.e., following ambient exposures to toxic and irritant pollutants from mobile and stack-emission sources), factors affecting aerosol deposition in the lungs of adolescents are issues of concern. As sulfate particles are natural products of the combustion of fossil fuels -- and are, therefore, consequences of many basic personal needs such as transporation and convenience (e.g., air-conditioning) and industrial and mining manufacturing uses, they are prevalent in the atmosphere. Hence, they cannot be avoided by the general public and workers.

In this work, we introduce hygroscopic growth information into a mathematical model describing aerosol deposition in the human lung. The results are intended for hazard evaluations pertinent to humans subsequent to exposures to pollutant atmospheres.

The influences of hygroscopic growth, taking place when inhaled particles enter the warm, moist human respiratory tract, are significant; and, should not be ignored in considerations of threat-to-human-health. We feel that our findings can be directed into aerosol therapy functions also, leading to more efficient administrations of drugs via the inhalation route. Therefore, our findings, considering age-dependency, are of potential application to pediatric medicine.

LUNG MORPHOLOGY

The human lung is a complex organ. A study of it, therefore, must be approached with a specific application in mind. For aerosol deposition modeling intents, it is necessary to assume an anatomical description of the lung within which particle motion is considered. Namely, airway dimensions (i.e., lengths and diameters) and spatial orientations (i.e., gravity and branching angles). Descriptions have ranged from the abstract branching schemes of Findeisen (1935) to those of Beeckmans (1965), Landahl (1950), Weibel (1963), and Yeh and Schum (1980). More elaborate, three-dimensional morphological definitions of the human lung, preceded by experimental studies with laboratory test animals (Mercer and Crapo, 1987) are forthcoming. The subject of lung physiology per se is beyond the scope of this paper; we shall only note that influences of different respiratory tract regions (Martonen, 1983a), and airway branching symmetry-asymmetry (Martonen and Gibby, 1982; Martonen, 1983b) have been considered elsewhere for inhaled particles and gases (Martonen and Wilson, 1982). In this effort, we shall perceive the geometry of the lung to be that as described by Weibel's Model A (1963). It is a symmetric, dichotomously branching network of airways, as presented in Table 1.

The airway generations, I, of the tracheobronchial (TB) region are numbered from 0 (i.e., the trachea) to 16 (i.e., the terminal conducting bronchioles), inclusive. The alveolated, pulmonary (P) airways are identified as generations 17 (i.e., the initial respiratory passages) to 23 (i.e., the alveolar sacs). The former have essentially an architectural, support role and the latter have primarily a gas-exchange function. A statistical variation of this morphology has been presented by Soong et al. (1979).

ENVIRONMENT OF THE LUNG

The environment within the human lung has not been thoroughly characterized; despite the fact that it will exert a primary influence upon the behavior and fate of inhaled particles -- of aerosol therapy and inhalation toxiclolgy concerns. Available data, descriptive of the lung, have been utilized by Eisner and Martonen (in press) in the design and development of a surrogate human lung.

The fluid dynamics and thermodynamics of the respiratory passages are two key elements in our modeling attempts. The kinetics of airflow in the lung has been a subject of a series of studies of Cambridge University's Physiological Flow Studies Unit, and these tasks have been reviewed by Pedley et al. (1977). With respect to aerosol deposition modeling, those results have been utilized in our laboratory in numerous investigations.

Regarding the heat and mass transport processes active in the respiratory tract, the subject has been overviewed by Morrow (1986). The temperature (T)

and relative humidity (RH) data that we have used in our calculations to simulate the warm, moist atmosphere of the human lung are presented in Figure 1. For inhalation via the mouth we consider air to be warmed to core body temperature (37°C) and 90% RH in the trachea. Then, we assume a monotonic increase of 1% in RH for each subsequent airway generation, until a saturation level of 99.5% is reached in generation I=10. For air that has been inspired via the nose, we consider humidification to be an RH of 99.5% in the trachea. These assumptions, admittedly simple, are consistent with the cited data. More research is obviously needed to systematically (i.e., airway-by-airway) categorize the T and RH of the human lung. Attempts to this end are active in our laboratory (Eisner and Martonen, submitted).

AEROSOL HYGROSCOPIC GROWTH DATA

The information which we shall use describing the hygroscopicity of atmospheric sulfuric acid particulate matter is that resulting from a series of laboratory research endeavors (Tang, 1976; Tang et al., 1977; Tang and Munkelwitz, 1977). In those works, the final, equilibrium sizes of sulfate pollutants (i.e., H_2SO_4, NH_4HSO_4, and $(NH_4)_2SO_4$) in controlled environments were measured. These data have been considered in earlier aerosol deposition modeling efforts (Martonen and Patel, 1981a, b). [Note: These determinations of ultimate particle growth are different from the measurements of growth rates, as quantitated by Bell and Ho (1981), Martonen et al. (1982), and Martonen and Lowe (1984). This is an important distinction, since the format in which hygroscopicity data is available dictates the manner in which particle growth effects within the lung can be mathematically simulated in aerosol deposition modeling purposes.]

In the cited Brookhaven National Laboratory publications, experimental measurements were augmented by theoretical modeling of hygroscopic particle mechanics, see Figures 6 and 8 of the Tang and Munkelwitz (1977) tests to which we refer the reader. Here, we shall accept the published growth description of sulfuric acid droplets, and consider it to be representative of ambient, toxic 'acid air'. The growth data have been incorporated, as computer subroutines, into our aerosol deposition model -- validated by comparisons of predicted deposition efficiences with laboratory test results with human test subjects, consider Martonen and Graham (1987a, b), -- to model hygroscopic effects.

Detailed, mechanistic theoretical analyses of hygroscopic growth continue to progress (Barrett and Clement, 1986). Such efforts we shall attempt to dovetail with experimental work in our laboratory (Eisner and Martonen, in press).

PARTICLE BEHAVIOR IN AIRWAYS

The primary deposition mechanisms in the lung are:

- o 'inertial impaction', occurring when a paricle's momentum is sufficient to cause its trajectory to deviate from a fluid streamline;
- o 'sedimentation', when a particle's motion is directed to an airway surface by the action of gravity; and
- o 'diffusion', or random Brownian motion.

These processes are illustrated in Figure 2.

The efficiencies of the deposition mechanisms are related to particle parameters such as size, shape and density. And, to respiratory parameters such as tidal volume and breathing rate, which determine an inhaled particle's velocity and influence its aerodynamic performance. The deposition probability equations used in this work are those presented by Martonen (1982); to give credit, formulas derived by other investigators are discussed therein.

The relative influences of less prominent forces on particle motion, such as thermal and electric sources, have been discussed in the textbook of Mercer (1973). Lately, Báláshazy et al. (submitted) have computed the effect of the 'interception' mechanism, and compared their work with cited texts -- relevant for fibrous particles, like asbestos. And, Martonen et al. (in press, a) have introduced the idea of 'cloud settling' in the lung, which may explain the predisposition of bronchogenic tumors in upper TB airways.

Since the aforementioned hygroscopic growth data have been published as the equilibrium size a particle attains when exposed to a specified T and RH environment, we must employ the data as prescribed. Hence, we assume that particle growth, and related deposition, occurs in a stepwise airway-by-airway fashion while traversing the lung.

Here, we focus upon breathing via the mouth -- because the laboratory data with which our mathematical model has been substantiated (Martonen and Graham, 1987a, b) is for oral exposures. [Note: the human test subjects have nose clips applied, to eliminate experimental artifacts arising from combined nose-mouth breathing]. We do appreciate that, in reality, humans

breathe through the nose and mouth; and indeed, this topic has been addressed in another peer reviewed publication (Miller et al., in press).

AEROSOL DEPOSITION COMPUTATIONS

There are considerable experimental data for the deposition of inhaled particles in the lung airways of adult humans. The subject is of importance to inhalation toxicology and aerosol therapy, and has been investigated by scientists from many countries (e.g., TGLD, 1966; Lippmann et al., 1971; Giacomelli-Maltoni et al., 1972; Foord et al., 1978; Hiller et al., 1982; Emmet et al., 1982; Svartengren et al., 1984; Heyder et al., 1986). But, only a paucity of deposition data has been published for children (Becquemin et al., 1987). Indeed, there has been only a modicum of airway dimensions per se characterized for children of various ages with enough detail to enable simulation of aerosol deposition (Hislop et al., 1972 and Phalen et al., 1985 for the TB region; Johnson et al., 1978 and Griscom and Wohl, 1985 for the trachea). There is limited data available to provide a model of children's airways proximal to the trachea. Therefore, we do not attempt to simulate deposition nor hygroscopic growth in the nose, mouth, or pharyngeal regions in this paper.

All of our simulations of the behavior and fate of inspired particulate matter are for a complete breathing cycle consisting of constant inhalation and exhalation flowrates, with no intermittent pauses. In this manner, our effort is

mathematically distinct from the modeling of Phalen et al. (1985) which considers deposition during the inspiratory portion of a breath only, thereby ignoring particle deposition during natural pauses and expiratory phases. In our calculations, deposition is normalized to the quantity of aerosol mass entering the trachea, as this is the format in which the experimental data are presented in the literature. [Note: deposition within the lung is not measured directly -- rather, it is inferred from time-lapse clearance studies. And, what is detected is the aerosol mass that has penetrated the oro-nasopharyngeal areas and entered the trachea.]

Airway dimensions for different subject ages are derived from Hofmann's (1982) equations for the TB region, and from Dunnill's (1962) data for the pulmonary region. See Martonen et al. (in press, b), and Ménache and Graham (in press), for a complete description of the methodology used to define the age-dependent human pulmonary region.

To compute the deposition efficiencies of inhaled particles, it is necessary to define appropriate respiratory parameters describing breathing cycles. In Table 2 the tidal volumes (TV) and breathing rates used in our calculations are stipulated, and appropriately referenced.

Figures 3 and 4 show total aerosol deposition as a function of particle diameter for both nonhygroscopic, iron oxide (Fe_2O_3) and hygroscopic, sulfuric acid (H_2SO_4) particles. And, for the five ages used in this study, for sedentary and maximal breathing modes, respectively. The Fe_2O_3 computations are 'controls' with respect to which hygroscopic effects may be determined. In

these graphs the abscissa is a particle's diameter in microns. Since above about 0.5 microns in actual (geometric) diameter, particle behavior is influenced by density and size, aerodynamic diameter is used. Particle behavior for particles smaller than approximately 0.5 microns in size is not influenced as much by density, so geometric diameter is used. In both cases, unless otherwise stated, particle diameter refers to the diameter of the particle immediately before it enters the human lung. For nonhygroscopic particles the size remains constant as it travels through the airways; for hygroscopic particles the size increases with water vapor uptake.

For resting, or sedentary, breathing it is apparent that the primary effect of hygroscopicity is to shift the deposition curves to the left. We note that for both the 'control' and 'acid air' calculations the families of age-specific deposition curves are parallel. For a given particle size deposition in the lung is greatest for the 7 month old subject and, for all practical intents and purposes, decreases monotonically as the lung develops during maturation. The minimum value of total deposition is shifted from about 1 micron to about 0.2 microns. Below 0.4 microns the effect of hygroscopicity is to decrease total deposition; above 0.4 microns the effect is to increase it: from about 1 to 2.5 microns hygroscopicity approximately doubles total deposition. This 'switch' in the rate of deposition can be attributed to the relative effectiveness of the deposition mechanisms of inertial impaction, sedimentation, and diffusion (Martonen et al., 1985).

For breathing at maximal activity, hygroscopicity has a similar overall effect, except that the 'cross-over' point between hygroscopic and

nonhygroscopic deposition is at approximately 0.3 microns. The minimum is shifted from a particle size of about 0.4 microns to 0.15 microns.

For sedentary breathing, the total deposition for a particle of any size is inversely related to age, primarily because younger lungs have smaller airways, and deposition is enhanced there. The wider separation of the adult curve from the others we attribute to the very low tidal volume chosen for the adult compared to those tidal volumes for the other ages. The same pattern occurs at maximal breathing: total deposition is inversely related to age. For maximal breathing however, the separation between ages is more uniform. It is interesting to note that hygroscopicity has an equal effect upon the curves for all ages; that is, the effect appears to be independent of age: e.g., the shift to the left for the 7-month-old is about the same as that of the adult.

Let us now address the question: what is the effect of the hygroscopic growth of 'acid air' within the human lung as related to health effects issues? Our computations demonstrate that the role of hygroscopicity -- for all human subject ages, as modeled in our work by considering an anatomically developing lung with approporiate respiratory parameters -- is a function of inhaled particle size. That is, the size of particle present in the pollutant atmosphere to which a population is exposed. For particles larger than certain limits, see Figures 3 and 4, growth promotes deposition. But, one must acknowledge that such particles will have been diluted upon the uptake of water vapor; thereby, perhaps reducing their toxicity and potential threat to lung tissues. For particles smaller than certain sizes, growth causes a reduction in deposition, henceforth lessening the initial burden delivered to the whole lung.

These effects do not appear to be a function of lung maturity as the age dependent deposition curves in Figures 3 and 4 are qualitatively the same.

CONCLUSION(S)

Aerosol deposition has been evaluated as a function of human subject age, and the hygroscopicity of inhaled particles. Results of our computations indicate that the growth of particulate matter within the lung is an important factor to be included into risk assessment protocols for inhalation exposures to atmospheric sulfates, and aerosol therapy regimens. We believe that 'acid air', with concomitant health effects issues, is a subject deserving increased attention, especially regarding damage to the developing human lung.

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FIGURE LEGENDS

Figure 1. A trimmed Weibel (1963) Model A tracheobronchial tree with measurements of temperature and relative humidity values of cited investigators.

Figure 2. Particle motion within lung airways, representing the deposition mechanisms of: 1) inertial impaction at a branching site, 2) sedimentation, and 3) diffusion.

Figure 3. Total aerosol mass deposited within the maturing human lung, normalized to the quantity entering the trachea on inspiration. Age dependent effects are plotted for nonhygroscopic (Fe_2O_3) and hygroscopic H_2SO_4) aerosols. Low activity, or sedentary, breathing conditions are considered.

Figure 4. Total aerosol mass deposited within the maturing human lung, normalized to the quantity entering the trachea on inspiration. Age dependent effects are plotted for nonhygroscopic (Fe_2O_3) and hygroscopic (H_2SO_4) aerosols. High activity, or maximal exertion, breathing conditions are considered.

TABLE 1

Airway dimensions of Weibel's (1963) Model A human lung morphology.

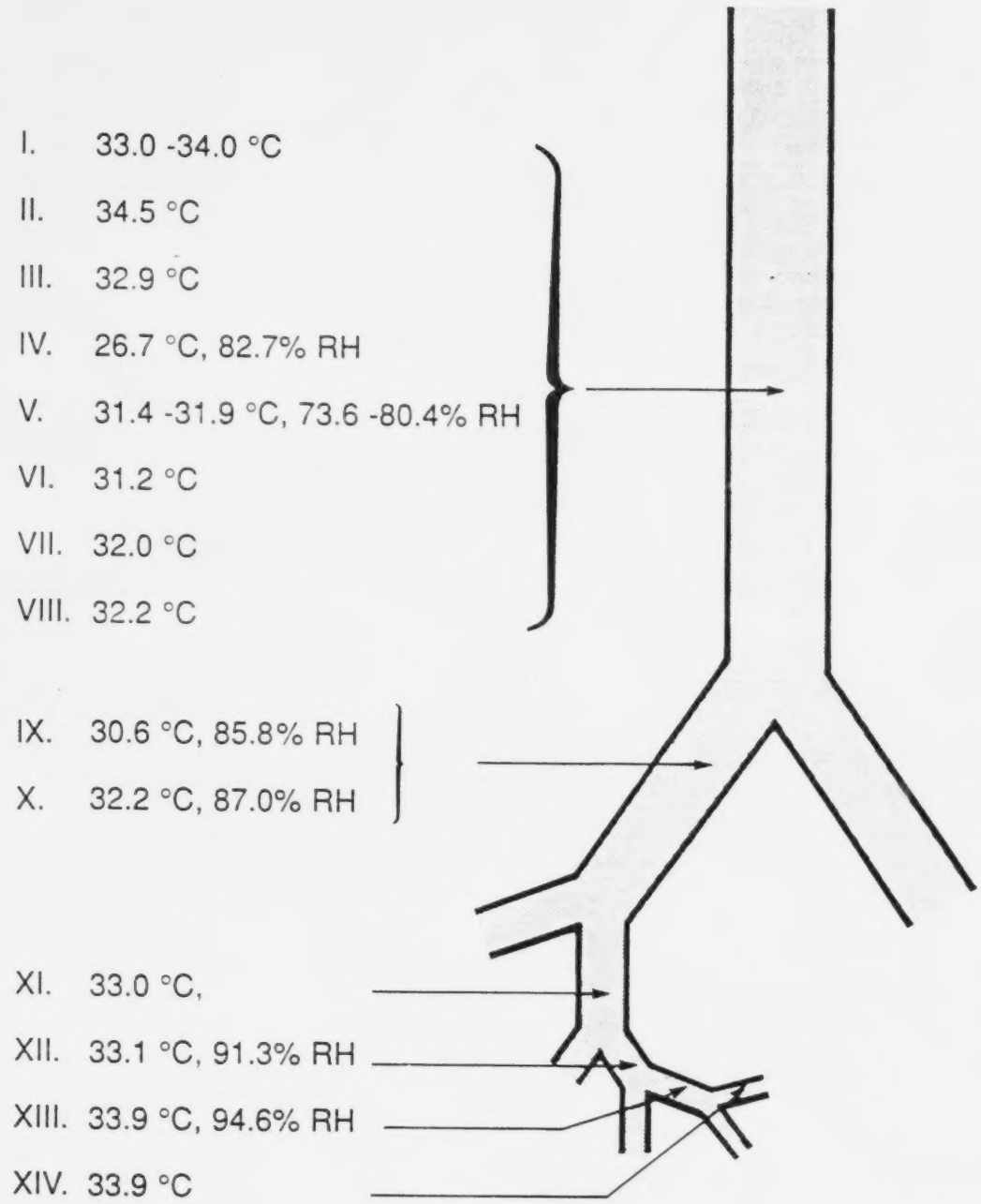
Generation, I	Diameter, cm	Length, cm
0	1.8	12.0
1	1.22	4.76
2	0.83	1.90
3	0.56	0.76
4	0.45	1.27
5	0.35	1.07
6	0.28	0.90
7	0.23	0.76
8	0.186	0.64
9	0.154	0.54
10	0.130	0.46
11	0.109	0.39
12	0.095	0.33
13	0.082	0.27
14	0.074	0.23
15	0.066	0.20
16	0.060	0.165
17	0.054	0.141
18	0.050	0.117
19	0.047	0.099
20	0.045	0.083
21	0.043	0.070
22	0.041	0.059
23	0.041	0.050

TABLE 2

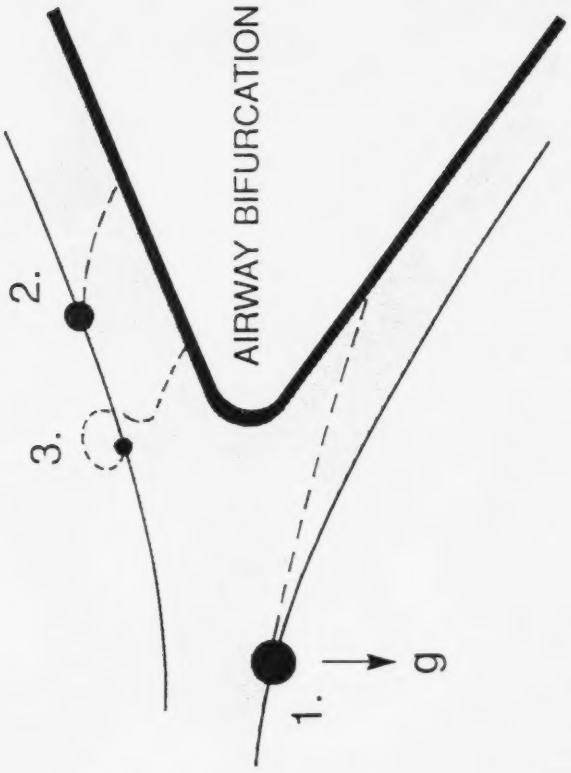
Age-dependent respiratory parameters chosen for aerosol deposition modeling in the developing human lung as a function of activity level.

Subject Age Months	Sedentary†		Maximal*	
	Frequency, breaths/min	Tidal Volume, ml	Frequency, breaths/min	Tidal Volume, ml
7	35	42	70	165
22	28	84	70	328
48	22	152	68	560
98	18	266	60	1190
Adult	14	500	40	3050

†Hofmann (1982)
*International Commission on Radiological Protection (1975)



I. Cole (1954)
II. Verzar et al. (1953)
III. Herlitzka (1921)
IV, VIII, XII. Déry et al. (1967)
V, IX, XIV. Déry (1973)
VI, VII, X, XIII. McFadden et al. (1985)


AIRWAY BIFURCATION
2.
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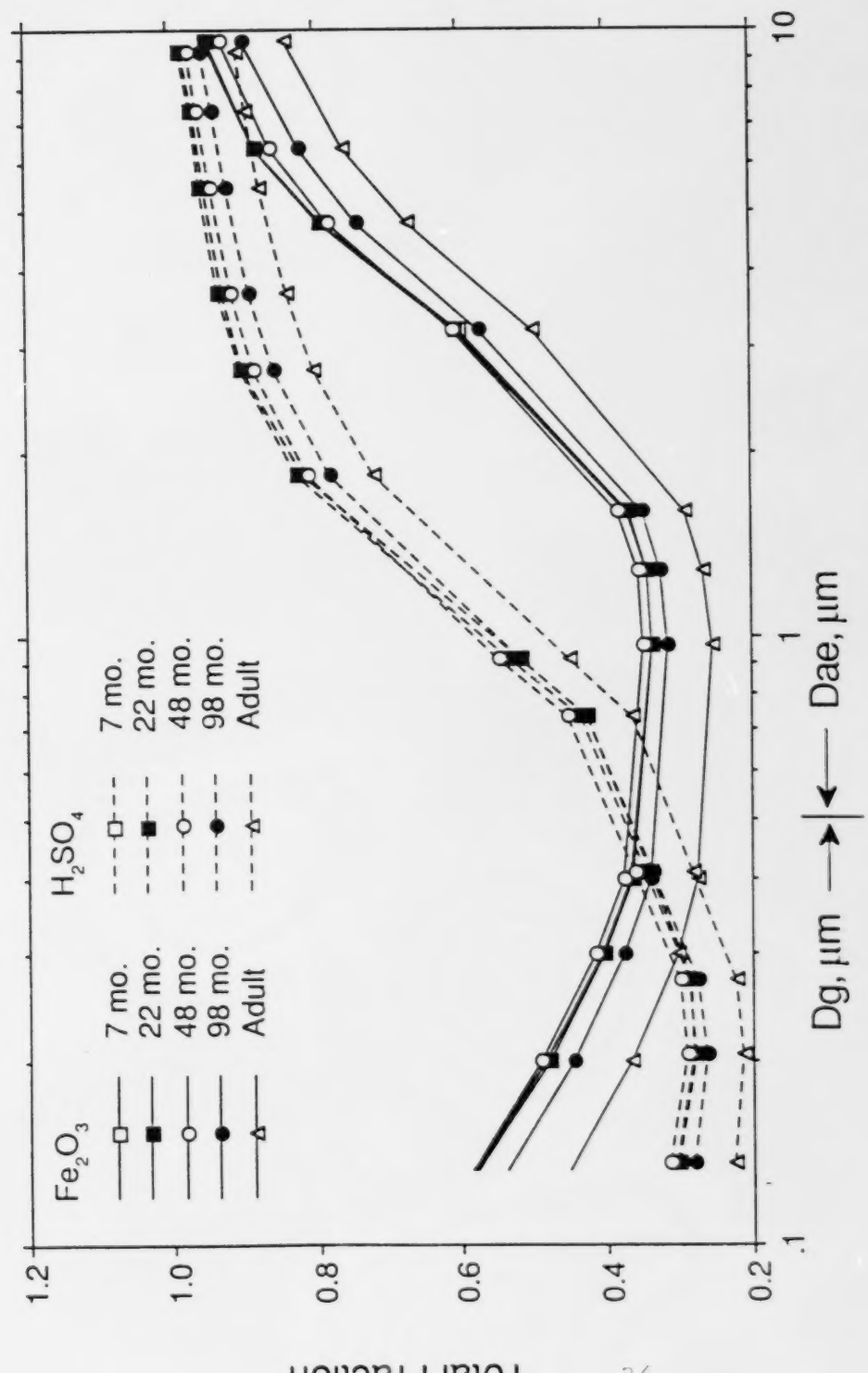
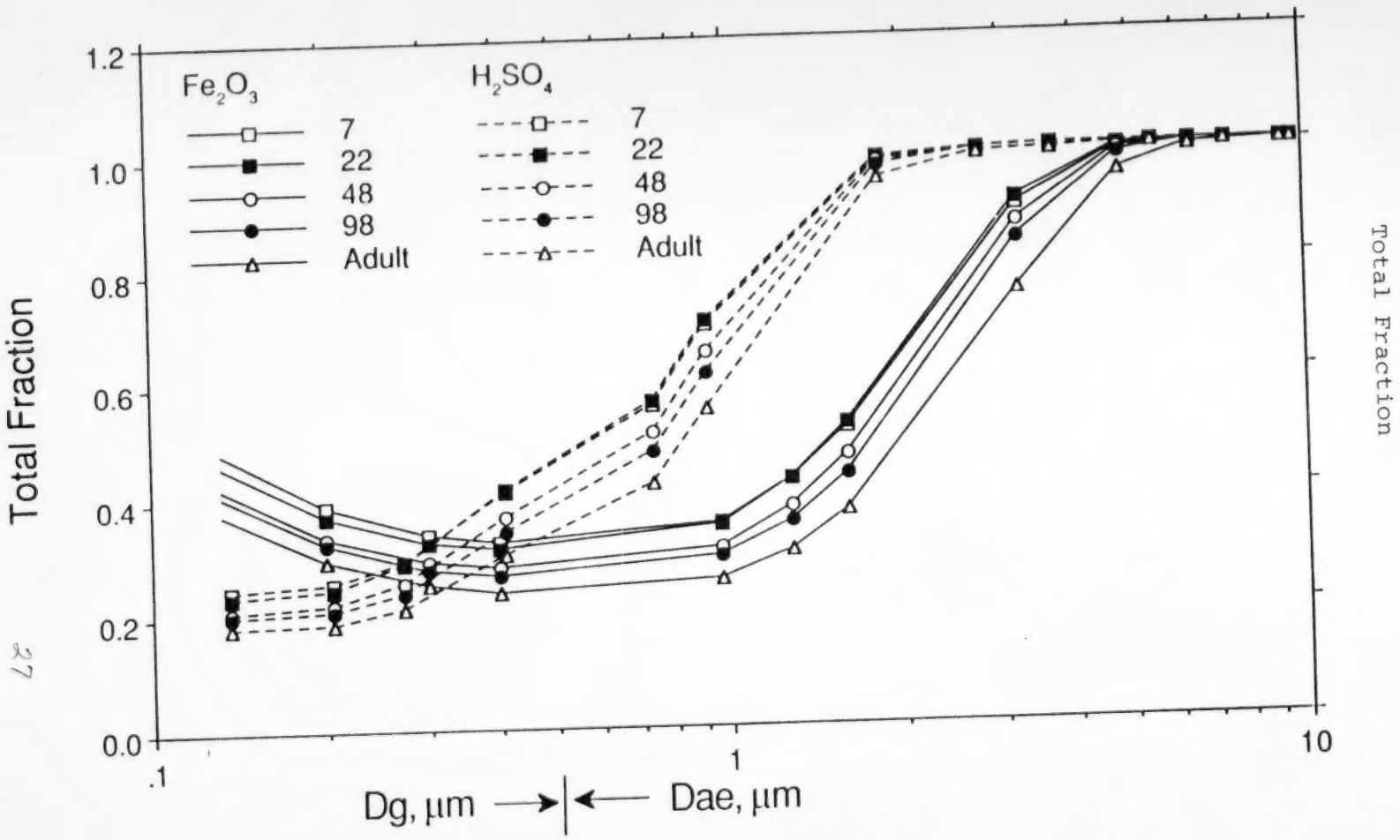

Fe2O3
7 mo.
22 mo.
48 mo.
98 mo.
Adult
H2SO4
7 mo.
22 mo.
48 mo.
98 mo.
Adult
1.2
1.0
0.8
0.6
0.4
0.2
.1
1
10
Dg, µm
Dae, µm
Total Fraction


Fe2O3
7
22
48
98
Adult
H2SO4
7
22
48
98
Adult
1.2
1.0
0.8
0.6
0.4
0.2
0.0
Total Fraction
.1
1
10
Dg, µm
Dae, µm
Total Fraction